with relative sparing of superior temporal and prefrontal regions. Logopenic PPA is associated with caudal temporal and inferior parietal atrophy. Seeds generated from these separate atrophy maps identify, in normal young individuals, two separate functional networks in resting-state functional connectivity analyses that mirror the normal dorsal fronto-parieto-temporal language network and the basal anterior temporopolar network in healthy adults. Formal convergence analyses are ongoing to quantify the extent of overlap between these maps. Preliminary analyses of longitudinal atrophy maps in PPA suggest that progression may proceed in a manner that respects network topography. **Conclusions:** Distinct clinical forms of progressive neurodegenerative aphasias appear to target two separable large-scale brain networks that are important for normal human communication abilities: a fronto-parieto-temporal network, regions of which are typically activated in fMRI language tasks, and a temporopolar network that is thought to be critical for multi-modal semantic knowledge. Convergent insights regarding the topography and functions of these language networks and their atrophy in PPA should provide the foundation for the development of novel biomarkers.

O1-05-05 THE CLINICAL PRESENTATION OF C9ORF72-ASSOCIATED FRONTOTEMPORAL LOBAR DEGENERATION IN AN EXTENDED FLANDERS-BELGIAN COHORT

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Background: Others and we recently identified pathogenic expansions of a hexanucleotide repeat in the gene C9orf72 as an important genetic cause of frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). The frequency of the C9orf72 mutation in the Flanders-Belgian FTLD cohort (n = 337) was 17% in familial and 4% in sporadic forms. **Methods:** We now aimed to define the distinguishing clinical and demographic features of FTLD caused by the C9orf72 repeat expansion. Phenotypic characteristics of 25 C9orf72 mutation carriers with FTLD were analyzed and compared to patients with GRN, MAPT and no know mutation. **Results:** The mean age at onset of disease in C9orf72 mutation carriers was 55 ± 7.8 range 42-69 years, which was earlier than GRN mutation carriers and mutation negative FTLD patients. The mean disease duration was 6.7 ± 4.6 range 2-17 years, similar to other patient groups. 87% was familial and 67% of C9orf72 families had a history of both FTLD and ALS. The most common clinical presentation seen in C9orf72 mutation carriers was behavioral variant FTLD with disinhibition as a frequent feature. Forms characterized by early apathy or non-fluent language dysfunction may also occur, but less frequently. ALS was significantly more frequent in FTLD with the C9orf72 mutation. However, the majority (68%) displayed no clinical signs of lower motor neuron disease. Non-fluent language presentation and limb apraxia were more common in GRN mutation carriers, while prominent behavior changes combined with semantic impairment was found in association with MAPT mutations. **Conclusions:** The clinical phenotype of C9orf72 repeat expansions was usually early onset behavioral variant FTLD with disinhibition as the dominant feature, occurring together with or without ALS. C9orf72 mutation carriers show differences in clinical characteristics compared to patients with mutations in other FTLD related genes. However, marked variation in the disease onset, course and clinical features are common.

O1-05-06 CHARACTERIZATION OF FRONTOTEMPORAL DEMENTIA +/- AMYOTROPHIC LATERAL SCLEROSIS ASSOCIATED WITH THE GGGGCC REPEAT EXPANSION IN C9ORF72

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Background: The gene responsible for familial frontotemporal dementia (FTD) +/- amyotrophic lateral sclerosis (ALS) on chromosome 9 (c9FTD/ALS) has been recently identified - the GGGGCC hexanucleotide repeat expansion in the noncoding region of C9ORF72. The antemortem and pathologic features associated with this mutation have not been well-characterized. **Methods:** All available clinical, inheritance, neuropsychological, neuroimaging and neuropathologic data on patients evaluated at Mayo Clinic in whom this mutation was identified were reviewed and analyzed. **Results:** Twenty-eight probands and 10 of their affected relatives were identified with the mutation; these and 10 additional affected relatives have been examined (total n = 48). Among these subjects, 27 (56%) were male. Age of onset ranged from 33 to 73 years (median 51 years) and survival ranged from 1 to 17 years (median 5 years). The age of onset was <40 years in 6 (13%) and >60 in 14 (30%). Clinical diagnoses included behavioral variant FTD (n = 30), ALS (n = 5), FTD/ALS (n = 10), and other syndromes (n = 3). Parkinsonism was present in 50% of subjects. No subject with a primary progressive aphasia diagnosis (n = 141) was identified with this mutation. Twenty-four (86%) of the 28 probands had an autosomal dominance pattern of inheritance. Incomplete penetrance was suggested in 2 kindreds, and the youngest generation had significantly earlier age of onset (>10 years) compared to the next oldest generation in 10 kindreds. The neuropsychological profile was that of slowed processing speed, complex attention/executive dysfunction, and impairment in rapid word retrieval. Neuroimaging studies showed bilateral frontal abnormalities most consistently, with variable degrees of parietal and temporal changes; no case had striking focal or asymmetric findings. Neuropathologic examination of 14 subjects revealed frontotemporal lobar degeneration with TDP-43-positive inclusions. **Conclusions:** Most cases with c9FTD/ALS have a characteristic spectrum of clinical, inheritance, neuropsychological, neuroimaging, and neuropathologic findings.